Investigation of Activities of Muscles for Opening Eustachian Tube as Assessed by Simultaneous Electromyography and Tympanic Air Exchange Observations

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Study Protocol

Protocol Title:	Investigation of Activities of Paratubal Muscles for Opening Eustachian Tube as Assessed by Simultaneous Electromyography and Tympanic Air Exchange Observations
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Study Coordinator:	None
Population:	14 participants. All participants are above the age of 18 and have been diagnosed with Normal Eustachian function. All are of Turkish descent.
Number of Sites:	Single site
Study Duration:	Data evaluation period: 1 month. Total duration: 9 months
Subject Duration:	45 minutes per subject.
Funding:	FUNDING. This work was supported by TUBITAK, Turkish Scientific and Technological Research Organization under grant 1120070.

General Information

Eustachian tube (ET) is a valve activated by levator and tensor veli palatine muscles and its duty is to equalize the pressure inside the tympanic cavity with outside pressure. Eustachian tube activation is commonly believed to be a sporadic activity which is initiated by swallowing or yawning action.

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Background Information

Although there have been numerous EMG studies to understand the synergistic behavior of the two muscles, these studies never revealed the periodic nature of the activity and the tight relationship between the two muscle signals in terms of amplitude and delay.

Objectives

This study focuses on the relationship between eustachian tube openings at rest and paratubal muscle functions by observing transpalatal electromyography (EMG) and actual tubometric air exchange activity in healthy individuals with normal eustachian tube function.

Study Design

The design of the study was to be open and uncontrolled. The expected duration of the study was 9 months with 55 participants. The study was only able to recruit 14 participants.

- Using EMG to measure the activity of the LVP and TVP as mLVP and mTVP.
- The Tubometric device was deemed to be very accurate.
- The study was deemed to be very safe, the tip of the measurement devices that were to be inserted in the mouth and ear were 1.3x0.4 mm sterile subdermal monopolar electrodes and caused no discomfort. It was judged that there was no need for anesthesia.

Study Population

- Patients older than 18 years of age and diagnosed with Normal Eustachian function.
- Inclusion criteria included Individuals with normal eustachian function whose eardrum is intact and no hearing problems.
- Exclusion criteria included: Patients with severe septal deformities, nasal polyps and turbinate hypertrophy, adenoid and other nasopharyngeal mass cases were excluded. Patients with upper respiratory tract infections, acute otitis media, timpanosclerosis, otosclerosis and those who had previous ear surgery were not included in the study group
- Furthermore, those who met the inclusion criteria were inspected for any additional undesirable factors, such as Patients diagnosed with major depressive disorder, dysthymic disorder, bipolar disorder Patients with asthma, heart failure, cardiac arrhythmia, Raynaud's phenomenon, peripheral artery disease, insulin dependent diabetes mellitus, sexual dysfunction, hypertension, and renal failure. If they had any of the conditions/disorders, they were disqualified from the study.
- The approval of the Local Clinical Research Ethics Committee was obtained to conduct this study in Haseki Training and Research Hospital. The ETDQ7 questionnaire was filled out in patients who came to the Otorhinolaryngology clinic of Haseki hospital and had various ear complaints. Patients with a score of 14.5 points or greater in this quantitative test were accepted as potential “chronic eustachian dysfunction patients, and all of them were tested by our audiometrist in the audiology laboratory.

Study Procedures

- It was scheduled for there to be one session per participant, with each session taking around 45 minutes to complete. In this timeframe a series of tests were conducted. In the first test, an appropriately sized ear silicon probe was placed and fixed in the ear canal as it is done in tympanometry tests. The subject was asked to take a sip of water in his/her mouth and hold it for a short amount of time. A nasal silicone probe was then placed on the opposite side of the nostrils gently but tightly. The subject was asked to obstruct the other nostril with his/her index finger while holding the probe in place securely and asked to swallow the water during the next ten seconds. Both ear canal and nasal pressure values were simultaneously recorded on tubometry computer for subsequent analyses.
  In the second test, another set of tubometry measurements was obtained from the patient while simultaneously recording EMG activities of mLVP, mTVP and external ear pressure of the ear. This time, the nasal probe was not used, and subjects were not asked to swallow water during the test. Since there was no swallowing action by the subjects, all eustachian tube opening activity was expected to be due to involuntary muscle activities of the ET

Using a "Tubometry" device to detect the minimal movement of the eardrum towards the outer ear canal we recorded this with a pressure sensor firmly placed in the outer ear canal. Simultaneously we detected and measured the movement of the muscles using an EMG with the results being recorded on a laptop with EMG Medelec ®Synergy was used for recording EMG activity of ET muscles in all the subjects.

- Furthermore, a routine biochemical analysis and hemogram was assessed.
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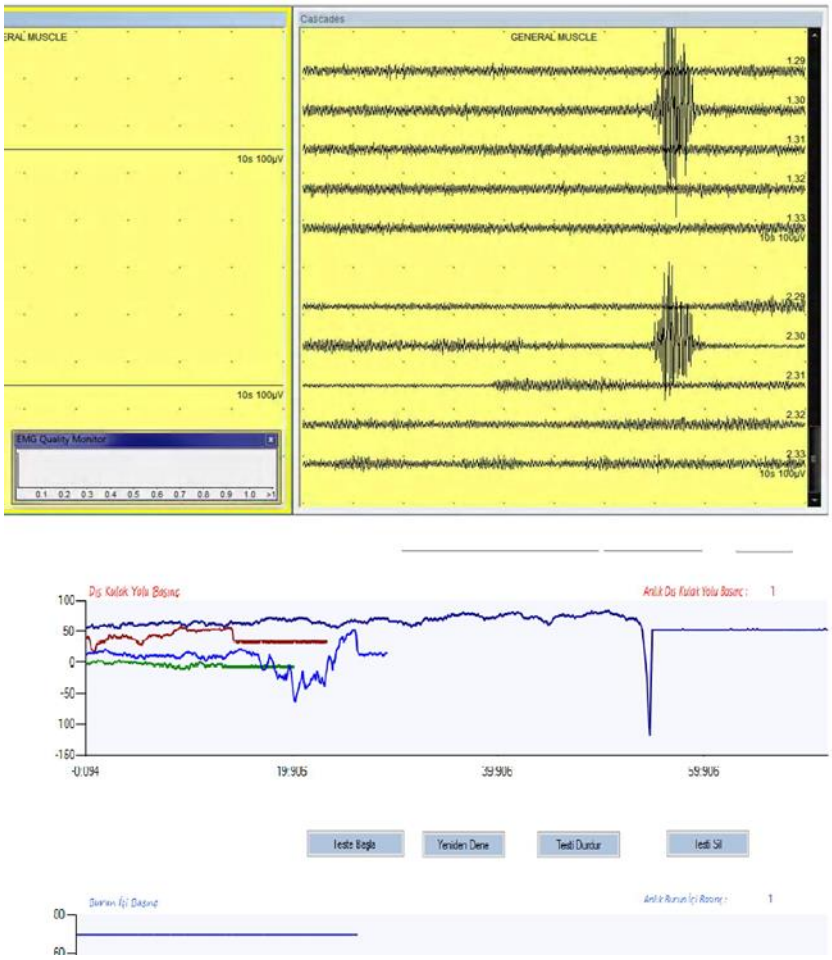

Figure. Simultaneous mLVP, mTVP and tubometry outputs for patient S.L recorded in one session. The simultaneous action of mLVP and mTVP opens the ET tube where the negative peak of tubometry indicates air being exhausted from TC. Since there was no swallowing action during the recording, opening action is solely due to muscle activity. Negative peak is interpreted as air leaving the cavity.

Data and Safety Monitoring

Results

A total of sixteen participants was included in the study with the gender distribution of 12 female and 4 male. The mean (SD) age of the subjects was 36.2 years (range 18-62 years). For one of the participants EMG recording was not obtained because of repetitive electrode dislodgment (possibly due to inadvertent swallowing activity). We attribute this failure to excessive saliva collected in the mouth. Another participant refused the needle insertion due to anxiety of needle fear. Thus, in 14 participants (mean age 36 years; 10 female and 4 male) EMG recordings with simultaneous tubometry data were obtained for both mLVP and mTVP.

Tubometry measurements were performed twice for every patient. First, the subjects were tested for the swallowing

efficacy of the ET opening. Second, the test was done withouwing activity while EMG activity of the muscles were recorded while observing ET openings on tubometry instrument. The measured pressure values obtained from the second test were used for calculating the amount of air entering or exiting the tympanic cavity.
The purpose of second tubometry testing was to observe and record the ET openings corresponding to concurrent EMG activities of the mLVP and mTVP with no swallowing action whatsoever. EMG and tubometry tests were performed and recorded by two different computers which were not linked to each other. Both instruments were started simultaneously at the same time to ensure synchronous operation. During the test, tubometry test device recorded pressure measurement of external ear canal only. Recording of nasal pressure is not done due to absence of swallowing activity. EMG recording device was operated in "continuous" mode where the data coming from the muscles were recorded continuously. Both EMG recordings and tubometry recordings were taken from the same ear undergoing the test. Analyses of the observed and recorded data revealed that only the double muscle activities of both mLVP and mTVP happening simultaneously were effective in opening ET. Isolated activities of either mLVP or mTVP were not effective for the ET openings in tubometry.
Figure shows the simultaneous mLVP, mTVP action of patient S.L for a healthy right ear as recorded by EMG and tubometry instruments. During testing no swallowing was allowed (Patient cannot swallow due to the electrodes in the mouth.) The EMG recording is done for duration of 200+ seconds. EMG screen in the Figure 5 is numbered to explain the recording. Due to the lengthy nature of the recording, the signal is recorded sequentially in the lines which are indicated as 1, 2, 3 and so on. The upper portion of the screen shows mLVP signal, whereas the lower one shows mTVP signal. Both signals are recorded simultaneously, and time reference is the same. As it can be seen from the figure, mLVP, mTVP activity starts during the latter part of the second line. This signal pattern occurs independent of swallowing action. The tubometry signal is recorded independently by another computer. Both EMG and tubometry recordings were started simultaneously. The tubometry screen shows a negative peak at t=51 seconds while EMG computer screen show a simultaneous burst mLVP and mTVP signals. Curiously, the peak appears as negative, which indicate air leaving the TC as ET opens. The negative nature of the pulse caused some confusion in the researchers in the beginning since it appeared in many other patients as well. Clearly, the negative pulse was not a fluke. Negative pulse seen on the tubometry screen is interpreted as air coming out of tympanic cavity as ET opens. We interpret this phenomenon as "air forced into a TC cavity during earlier swallowing" exiting the TC cavity. Although not shown in the figure, subsequent sets of mLVP, mTVP burst that came after the first set, did not cause a negative peak. This is interpreted as, "although ET opens, since pressure inside the TC is stable no air exchange occurs".

Table 1. Summary results for each recorded variable of the EMG activities of the right mLVP and mTVP opening the ET in tubometry.

Patient	**Gender, age**	**1.tymp**	**2.tymp**	**Latency (ms)**	**mLVP amp(µV)**	**mTVP amp(µV)**	**Intervals(s)**	**Ratio**
1	*M,35*	*L-20,R-8*	*L-48,R-24*	*130*	*436.3*	*194.4*	*26.6*	*2.24*
2	*F,34*	*L-48,R-36*	*L-36,R-40*	*106*	*495.8*	*180.3*	*20*	*2.8*
3	*F,19*	*L-32,R-44*	*L-56,R-44*	*221*	*444.7*	*175*	*15*	*2.54*
4	*F,33*	*L-44,R-68*	*L-44,R-64*	*200*	*376.6*	*213*	*24*	*1.84*
5	*F,44*	*L-36,R-28*	*L-40,R-40*	*240*	*378*	*205*	*7*	*1.84*
6	*F,18*	*L-80,R-64*	*L-48,R-52*	*170*	*608*	*1033*	*2*	*0.6*
7	*F,49*	*L-44,R-36*	*L-44,R-48*	*100*	*265.05*	*84.2*	*16.6*	*3.1*
*8**	*M,33*	*L-148,R-28*	*L-148,R-28*	*122.8*	*192.7*	*82.4*	*17.1*	*2.36*
9	*F,23*	*L-112,R-36*	*L-110,R-40*	*100*	*667*	*539*	*10.7*	*1.25*
10	*M,62*	*L-60,R-160*	*L-66,R-45*	*123*	*876*	*443.9*	*9.3*	*1.98*
11	*F,55*	*L-76,R-*	*L-68,R-44*	*63.3*	*506.7*	*390*	*22.8*	*1.3*

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12	*F,38*	*L-184,R-60*	*L-76,R-64*	*0*	*190*	*120*	*19*	*1.5*
13	*M,32*	*L-32,R-40*	*L-44,R-40*	*92.5*	*111.7*	*93*	*50*	*1.20*
14	*F,32*	*L-36,R-40*	*L-40,R-44*	*120*	*133*	*181.7*	*26*	*0.73*

Latency (ms): Latency (millisecond), Tymp: Tympanogram, mLVP amp: Amplitude of LVP muscle (microvolt), mTVPamp: Amplitude of TVP muscle (microvolt), Interval(s): Interval (seconds), Ratio: Ratio of the amplitudes of mLVP/mTVP

- Adverse events were not expected as the procedure was evaluated as being very safe.
- In the event of any expected adverse events, the impact of the event was to be discussed internally.
- The safety evaluation of the test was done as a periodic review by the research team itself.

Statistics

- All eligible participant data is to be used in the analysis. On the subjects themselves it was planned for there to be 55 participants, but the research team could only recruit 14. Larger population was deemed an appropriate number for the trial to be clinically significant.
- The trial was to be terminated if the subjects showed any sign of fear or panic during the trial.

Ethics

- Permission from a local review board (SAB HASEKI EGTIM VE RASTIRMA HASTANESI) was sought and approved.
- Subjects were asked to sign a consent form, the forms themselves are stored securely and subjects to be referred to by number, rather than by name.

Data handling and record keeping

- Source documents are stored on a secure computer in the EMG lab, subjects are unlikely to be identified using the information as the subjects are referred to only by number and gender.
- The sponsor inserted a member into the team to ensure quality control and record retention.

Quality control and assurance

- Self-assessment was used to ensure the quality and reliability of the data, there are currently plans to involve a third party for further assurance.

Publication Plan

- There are plans to publish the results in larger series study on PubMed.
- The results will not be returned to the subjects.